K131791

EUROIMMUN US

FEB 2 6 2014

PREMARKET NOTIFICATION
510(K)
SAFETY AND EFFECTIVENESS SUMMARY
(as required by 21 CFR § 807.92)

A. 510(k)Number:
K131791

B. Purpose for Submission:
New device

C. Measurand:
Anti-nuclear autoantibodies (ANA)

D. Type of Test:
Qualitative and/or Semi-Quantitative, indirect immunofluorescence

E. Applicant:
EUROIMMUN US INC.

F. Proprietary and Established Names:
EUROIMMUN IFA 40: HEp-20-10

G. Regulatory Information:

1. Regulation:
   21 CFR 866.5100 - Antinuclear antibody immunological test system
2. Classification:
   Class II
3. Product code:
   DHN
4. Panel:
   Immunology

H. Intended Use:

1. Intended Use(s):
   The EUROIMMUN IFA 40: HEp-20-10 is an indirect immunofluorescence antibody test for the qualitative or semi-quantitative detection of antibodies against cell nuclei (ANA) in human serum. This test system is used as an aid in the diagnosis of systemic rheumatic diseases in conjunction with other laboratory and clinical findings.
2. Indication(s) for use:
   Same as Intended Use.
3. Special conditions for the use statement(s):
   For Prescription Use Only.
4. Special instrument requirements:
   Fluorescent Microscope: Equipped with a 488 nm excitation filter; 510 nm color separator; & 520 nm blocking filter with a 100 W mercury vapour lamp light source or LED bluelight.

I. Device Description:
The test system consists of BIOCHIPs coated with HEp-20-10 cells. It includes a fluorescein-labeled goat anti-human IgG, a positive and negative control, salt for PBS, Tween 20, embedding medium, cover

glasses and instruction booklet. Reagent trays for the TITERPLANE technique are required but ordered separately.

J. Substantial Equivalence Information:

1. Predicate device name (s):
   ImmunoConcepts® Hep-2000 ANA-Ro IFA
2. Predicate 510(k) number(s):
   K972145
3. Comparison with predicate:

Similarities

Item	New device	Predicate device
Intended use	Qualitative or semi-quantitative detection of antibodies against cell nuclei (ANA). The test system is used as an aid in the diagnosis of systemic rheumatic diseases, in conjunction with other laboratory and clinical findings.	Same
Samples	Serum 1:40 dilution	Same
Technology	IFA	Same
Reagents	Fluorescein HEp-20-10 cultured cells	Fluorescein HEp-2000 cultured cells
Procedure	Standard IFA technique; serum incubation with cells, followed by a wash step, incubation with fluorescein–labelled anti–human globulin, wash step, embedding and reading fluorescence with a fluorescence microscope.	Same
Cut off level	1:40 dilution	Same
Reported results	qualitative, Titer	Same

Differences

Item	New device	Predicate device
Technology	BIOCHIP TITERPLANE technology HEp-20-10 cells are bound to the BIOCHIPs	Standard IFA technology HEp-2000 cells are bound to the test wells
Controls	1 Positive control 1 Negative control	5 Positive controls (one each for the following patterns: SSA/Ro, homogeneous, speckled, nucleolar, centromere) 1 Titratable control serum 1 Negative control serum

K. Standard/Guidance Document Referenced (if applicable):

Guidance for Industry and FDA Staff: Recommendations for Anti-Nuclear Antibody (ANA) Test System Premarket (510(k)) Submissions (January 22, 2009)

L. Test Principle:

The principle follows the TITERPLANE technique. Patient samples, controls and in separate steps conjugate and embedding medium are applied to the reaction fields of a reagent tray. The BIOCHIP Slides are then placed into the recesses of the reagent tray, where all BIOCHIPs of the slide come into contact with the fluids, and the individual reactions commence simultaneously. The fluids are confined to the recessed wells eliminating the need to use a conventional "humidity chamber".

Patient samples are diluted 1:40 in PBS-Tween, 30 µl of each diluted patient sample are added to each reaction field of the reagent tray. Reactions are started by fitting the BIOCHIP Slides containing the sections from the substrate (HEp-20-10 cells) into the corresponding recesses of the reagent tray and incubated for 30 minutes at room temperature. Specific antibodies attach to the HEp-20-10 antigens. After incubation the BIOCHIP Slides are washed with PBS-Tween to remove unbound antibodies. In the meantime, 25 µl of fluorescein–labelled anti–human globulin are added to each reaction field of a clean reagent tray and the BIOCHIP Slides placed into the recesses of the tray. After a 30 minutes incubation at room temperature, the BIOCHIPs are again washed with PBS-Tween to remove any unbound fluorescein-labelled reagent. 10 µl of Embedding medium are placed for each reaction field on a cover glass and the BIOCHIP Slides, with the BIOCHIPs facing downwards, placed onto the prepared cover glass. Fluorescence is read with a fluorescence microscope.

M. Performance Characteristics (where applicable):

1. Analytical performance:

General: The fluorescence intensity level is the intensity of the specific fluorescence expressed as a numeric value. These values can vary from "0" (no specific fluorescence) to "4+" (strong specific fluorescence). The evaluation of the fluorescence intensity is performed according to the following table:

Intensity	Evaluation
0	Negative: No specific fluorescence.
1+	Positive: weak visible reaction; dim subdued fluorescence. (Cut-off)
2+	Positive: Moderate visible reaction; green fluorescence.
3+	Positive: Strong visible reaction; brilliant green fluorescence
4+	High Positive: Very strong visible reaction; brilliant green (maximal fluorescence).

A serum dilution is considered negative for ANA antibodies if the cells exhibit < 1+ fluorescence and no discernible pattern. Likewise, a serum dilution is considered positive for ANA antibodies if the cells exhibit ≥ 1+ fluorescence and a discernible pattern. A sample is considered positive for ANA antibodies if it exhibits ≥ 1+ fluorescence and a discernible pattern at a sample dilution of 1:40 or greater. Technicians should report all titers and patterns seen.

a. Precision/Reproducibility:

Reproducibility was investigated using a panel of serum samples representing the range of patterns at different intensities. All analytical performance studies were performed at EUROIMMUN Medizinische Labordiagnostika AG, Lübeck, Germany, if not stated otherwise.

Intra-Assay Reproducibility was determined by 10 fold repeated measurements in one run. The EUROIMMUN IFA 40: HEp-20-10 assay was processed according to the package insert and evaluated by the same technician. The results of the different assays did not exceed the acceptable deviation of fluorescence intensity of +/- 1 intensity level, positive samples were not found negative and vice versa, and the observed patterns did not change.

Inter-Assay Reproducibility was determined by 20 repeated measurements on 5 different days with 2 runs per day and 2 replicates per run. The EUROIMMUN IFA 40: HEp-20-10 assays were processed according to the package insert and evaluated by the same technician. The results of the different assays did not exceed the acceptable deviation of fluorescence intensity of +/- 1 intensity level, positive samples were not found negative and vice versa, and the observed patterns did not change.

Inter-Lot Reproducibility was determined by 6 repeated measurements with 3 different lots, 1 run per lot, 2 replicates per run. The EUROIMMUN IFA 40: HEp-20-10 assays were processed according to the package insert and evaluated by the same technician. The results of the different lots did not exceed the acceptable deviation of fluorescence intensity of +/- 1 intensity level, positive samples were not found negative and vice versa, and the observed patterns did not change.

Inter-Observer Reproducibility was determined by separate independent reading of the Inter-Assay slides by a 2nd technician. In case of discrepancies a 3rd technician would have been decisive. The results of the different assays did not exceed the acceptable deviation of fluorescence intensity of +/- 1 intensity level, positive samples were not found negative and vice versa, and the observed patterns did not change. The Inter-Observer Reproducibility Study was performed in a US Laboratory setting.

Semi-quantitative Reproducibility was determined by measurements of dilutions (1:40 up to 1:40960) of 14 positive samples and a negative sample, covering the 7 main patterns (homogeneous, granular, nucleolar, centromeres, nuclear dots, nuclear membrane and cytoplasmic), with fluoresence intensities ranging from 1+ to 4+. The samples/dilutions were assayed in 4 different runs, performed with 3 different lots, in duplicates. The EUROIMMUN IFA 40: HEp-20-10 assays were processed according to the package insert and evaluated by two different technicians. The results of the different assays for each dilution did not exceed the acceptable deviation of fluorescence intensity of +/- 1 intensity level, so the endpoint titer did not deviate more than +/- 1 titer level, and the observed patterns did not change.

b. *Linearity/assay reportable range:*
An assay with a semi-quantitative claim should demonstrate that samples will decrease in fluorescence intensity with increasing dilutions. To demonstrate this several samples (6) with different combinations of mixed staining patterns were serially diluted and evaluated/tested with the EUROIMMUN IFA 40: HEp-20-10 assay. The samples were assayed according to the package insert. Each sample/dilution combination was tested and the fluorescence intensity and pattern were recorded.

Mixed patterns could be distinguished in every dilution, and the samples showed a decrease in fluorescence intensity as the samples were diluted. The pattern of the samples did not change with dilution. Acceptable deviation of fluorescence intensity: ± 1 intensity level.

c. *Traceability, Stability, Expected values (controls, calibrators or methods):*
A recognized standard or reference material for Anti-Nuclear Antibodies is not available.

Negative and positive controls are included in the kit, Ready for Use. The negative control should exhibit less than 1+ or .no specific fluorescence (autoantibody negative). The positive control should exhibit a homogenous staining pattern with a fluorescence intensity of >1+ (3-4+). The homogenous pattern of the positive control was confirmed via testing. EUROIMMUN Inc. recommends using the positive and negative controls as stated within the labeling (Instructions for Use).

The EUROIMMUN IFA 40: HEp-20-10 kit is stable for a period of 18 months after the date of manufacture if stored properly. As the composition of the EUROIMMUN IFA 40: HEp-20-10 kit is very similar to the EUROIMMUN ANA IFA: Hep-20-10 kit, stability of most components have already been demonstrated in the K070763 510(k) process. Real time stability tests of the "new" component (conjugate) as well as for the entire kit are conducted in accordance with the international standard DIN EN 13640:2002: Stability testing of in vitro diagnostics reagents. Three production lots of all kit reagents are tested.

d. *Limit of detection:*
Not applicable.

e. *Analytical specificity:*
Cross-reactivity: The specificity of the EUROIMMUN IFA 40: HEp-20-10 was verified using the ANA reference panel of the CDC Centers for Disease Control and Prevention, Atlanta, USA. The CDC samples were assayed according to the package insert by the same technician at the same day. The results are in line with the characterization by the CDC with the exception of CDC sample No. 12. This sample was also tested using the EUROIMMUN ANA IFA: HEp-20-10 (K070763) and the ImmunoConcepts® HEp-2000 ANA-Ro IFA (K972145). The sample was found negative with all three test systems.

In addition to the CDC panel, clinical samples positive for ANCA-associated vasculitis, Crohn's disease, ulcerative colitis, celiac disease and infectious diseases (Chlamydia pneumoniae and Epstein-Barr virus) (each 10 samples) were investigated. The results do not indicate any significant cross reactivity.

Interfering substances: The effect of interfering substances on assay results were tested by spiking 20 clinical samples with hemoglobin (0, 250 & 500 mg/dL), bilirubin (0, 10 & 40 mg/dL) and triglycerides (0, 500 & 2000 mg/dL). The samples consisted of negative (< 1:40), weak positive and strong positive samples with varying pattern specificities. Interferences from human anti-mouse antibodies (HAMA) and rheumatoid factor (RF) was tested by diluting these samples 1:1 with high positive HAMA serum or a high positive RF serum respectively. The spiked samples were incubated with the EUROIMMUN IFA 40: HEp-20-10 according to the package insert by the same technician on the same day. The deviation in fluorescence intensity level did not exceed +/- 1. The results indicated that hemoglobin (up to 1000 mg/dl), bilirubin (up to 40 mg/dl), triglyceride (up to 2000 mg/dl), HAMA and RF at the concentrations indicated have no effect on assay results. No significant interference was observed.

f. *Assay cut-off:*
The recommended starting dilution, above which the result is reported as positive and below which the result is reported as negative, is 1:40. The manufacturer suggests performing four-fold

dilutions but recommends that each laboratory establish its own titering protocol. The titers of 1:40 and 1:80 are considered low titers, 1:160 and 1:320 are considered medium titers, and 1:640 and greater are considered high titers. Assay cut-off of 1:40 was determined from the literature, see:

Tan, EM, Feltkamp TEW, Smolen J S, Butcher B, Dawkins R, Fritzler MJ, Gordon T, Hardin JA, Kalden JR, Lahita RG, Maini RN, McDougal JS, Rothfield NF, Smeenk RJ, Takasaki Y, Wiik A, Wilson MR, Koziol JA. *Range of antinuclear antibodies in "healthy" individuals.* Arthritis & Rheumatism 40 (1997) 1601–1611. doi: 10.1002/art.1780400909

Arthur Kavanaugh, MD; Russell Tomar, MD; John Reveille, MD; Daniel H. Solomon, MD, MPH; Henry A. Homburger, MD. *Guidelines for Clinical Use of the Antinuclear Antibody Test and Tests for Specific Autoantibodies to Nuclear Antigens.* Arch Pathol Lab Med. 124 (2000) 71 – 81.

A prospective study was performed at EUROIMMUN US Inc. laboratory to verify the cut-off using a total of 138 samples. The serum samples sent in for antibody testing were collected in sequential order for two days and considered for the study if age and sex data were available. The panel consisted of samples from 53 men and 85 women submitted for a routine health screening. Age ranged from 0 to 89 years with an average age of 51 years. Testing, at initial dilution of 1:40, was performed as per the Instructions for Use. 16 of the 138 samples were found positive for anti-nuclear antibodies using the EUROIMMUN IFA 40: Hep-20-10 kit, resulting in a prevalence of 11.6% (95% C.I.: 6.8% – 18.6%). As per the American College of Rheumatology a prevalence of ANAs in healthy individuals is about 3.0 - 15%.

2. Comparison studies:

a. Method comparison with predicate device:

Qualitative: A comparison study was performed using a cohort of 200 blinded prospective samples from the Department of Clinical Pathology & Laboratory Medicine at the University of Pennsylvania. Samples obtained from patients sent for routine ANA screening, where at minimum age and sex was available. The samples were tested with EUROIMMUN HEp-20-10 IFA 40 concurrently with ImmunoConcepts® HEp-2000 ANA-Ro IFA (K972145) (predicate). The panel consisted of 59 men and 141 women. Age ranged from 19 to 89 years with an average age of 52 years. The tests were performed according to the package insert (1:40 Dilution) in single determinations. Visual fluorescence microscopy evaluation was performed by two different technicians independently. In case of a discrepant result a 3rd technician was decisive.

n = 200		ImmunoConcepts® HEp-2000 ANA-Ro IFA		
		Positive	Negative	Total
EUROIMMUN IFA 40: HEp-20-10	Positive	61	6	67
	Negative	5	128	133
	Total	66	134	200

% Negative Agreement	128/134	= 95.5%	95% C.I.:	90.5%	-	98.3%
% Positive Agreement	61/66	= 92.4%	95% C.I.:	83.2%	-	97.5%
% Overall Agreement	189/200	= 94.5%	95% C.I.:	90.4%	-	97.2%

Of the 6 discrepant positive samples: All 6 samples were reported by Univ. of Penn. as positive samples. (4 homogenous, >1:160; 1 nucleolar, 1:320; & 1 granular, 1:80 [SS-A+ Blot]).

Of the 5 discrepant negative samples: 1 sample was confirmed by blot as negative; 3 samples were reported by Univ. of Penn. as negative; and 1 sample was reported by Univ. of Penn. as speckled/granular and confirmed SS-A positive by blot.

Confirmations were done using FDA cleared assays.

Semi-Quantitative/Quantitative: A comparison study was performed using a cohort of 156 blinded prospective samples from samples obtained from patients sent for routine ANA screening, where at minimum age and sex was available. The samples were tested with EUROIMMUN HEp-20-10 IFA 40 concurrently with ImmunoConcepts® HEp-2000 ANA-Ro IFA (K972145) (predicate). The panel consisted 62 men and 94 women, average age of 52 yrs, age

ranged from 19 to 90 yrs. The tests were performed according to the package insert in single determinations. Visual fluorescence microscopy evaluation was performed by two different technicians independently. In case of a discrepant result a 3rd technician would have been decisive.

n = 156		ImmunoConcepts® HEp-2000 ANA-Ro IFA		
		Positive	Negative	Total
EUROIMMUN IFA 40: HEp-20-10	Positive	110	0	110
	Negative	0	46	46
	Total	110	46	156

% Negative Agreement	46/46	= 100.0%	95% C.I.:	92.3%	-	100.0%
% Positive Agreement	110/110	= 100.0%	95% C.I.:	96.7%	-	100.0%
% Overall Agreement	156/156	= 100.0%	95% C.I.:	97.7%	-	100.0%

Pattern agreement is tabulated below. A single staining pattern was seen with 79 samples, and mixed patterns were seen with 31 samples. For the table each was reported individually.

Observed Patterns

Pattern	n	EUROIMMUN IFA 40: HEp-20-10	ImmunoConcepts® Hep-2000 Fluorescent ANA-Ro	% Agreement
Homogenous	41	41	41	100.0
Granular/Speckled	28	28	26	92.9
Nucleolar	24	22	23	87.5
Centromere	15	15	15	100.0
Nuclear Dot	9	9	9	100.0
Nuc. Membrane	3	3	2	66.7
Cytoplasmic	28	26	28	92.9
			Overall % Agreement:	91.4

Comparison of reciprocal titers between the predicate and the new assay is shown below. If multiple patterns were reported, those titers are reported separately:

PREDICATE: Reciprocal Titer

EUROIMMUN	<40	40	80	160	320	640	1280	2560	5120	10,240	Total
<40	46		1[5]	2[3,7]							49
40			2								2
80		7	7	4							18
160	2[2,4]		18	13	7		2‡				42
320	2[1,6]			16	14	3		1‡			36
640					9	5	2	1‡			17
1280						4	6	3			13
2560							5	2	1	2‡	10
5120								3			3
10,240									1	2	3
Total	50	7	28	35	30	12	15	10	2	4	193

‡HEp-2000® Fluorescent ANA-Ro Test System [K972145] 02.24.1998: Because of the overexpression of the SS-A/Ro autoantigen in the HEp-2000® cells, samples that contain anti-Ro/SS-A antibodies show higher titer values on these cells than the values obtained on non-transfected HEp-2 cells. A distinct speckled and nucleolar pattern is seen in 10 - 20% of the interphase nuclei; some cells may show staining in the cytoplasm. These are the hyper-expressing cells. (ImmunoConcepts® N.A. Ltd, 2007)

[1]Sample No. 29: Granular/Speckled pattern observed with new device. Blot positive SS-A/Ro; [2]Sample No. 46: Granular/Speckled pattern observed with new device. Blot positive SS-A (++); [3]Sample No. 46: Cytoplasmic pattern observed with predicate device. Blot positive Sm (+) near Cut-off; [4]Sample No. 121: Nucleolar pattern observed with new device. Blot negative; [5]Sample No. 121: Cytoplasmic pattern observed with predicate device. Blot negative; [6]Sample No. 145: Nuclear Membrane pattern observed with new device. Blot positive Sm (+) near Cut-off; [7]Sample No. 146: Nucleolar pattern observed with predicate device. Blot positive SS-A (++).

b. Matrix comparison:

Not applicable.

3. Clinical studies:
   Not Applicable

   Other clinical supportive data:
   Not applicable.

4. Clinical cut-off:
   See Assay cut-off.

5. Expected values/Reference range:
   The reference range of ANA was analyzed with the EUROIMMUN IFA 40: HEp-20-10 kit. A panel of 200 sera from normal healthy adult blood donors of mixed age and gender (155 men, 45 women, mean age 38 years, age range 18-68 years), originated from the University hospital Lübeck, Germany. The samples were assayed according to the package insert at the same day by three technicians. Prevalence of ANA was found about 3.5%. As per the American College of Rheumatology a "prevalence of ANAs in healthy individuals is about 3.0 - 15%". The reference range was determined as titer <1:40.

N. Proposed Labeling:
The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:
The submitted information in this premarket notification is complete and supports a substantial equivalence decision.

Michael Locke	Dir. Of Regulatory Affairs	17 February 2014
Signature	*Title*	*Date*

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

February 26, 2014

EUROIMMUN US
MR. MICHAEL A LOCKE
DIRECTOR OF REGULATORY AFFAIRS
1100 THE AMERICAN ROAD
MORRIS PLAINS NJ 07950

Re: k131791
Trade/Device Name: EUROIMMUN IFA 40: HEp-20-10
Regulation Number: 21 CFR 866.5100
Regulation Name: Antinuclear antibody immunological test system
Regulatory Class: II
Product Code: DHN
Dated: January 29, 2014
Received: January 30, 2014

Dear Mr. Locke:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Maria M. Chan -S

Maria M. Chan, Ph.D.
Director
Division of Immunology and Hematology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement on last page.

510(k) Number *(if known)*
K131791

Device Name
EUROIMMUN IFA 40: HEp-20-10

Indications for Use *(Describe)*
The EUROIMMUN IFA 40: HEp-20-10 is an indirect immunofluorescence antibody test for the qualitative or semi-quantitative detection of antibodies against cell nuclei (ANA) in human serum. This test system is used as an aid in the diagnosis of systemic rheumatic diseases in conjunction with other laboratory and clinical findings.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON A SEPARATE PAGE IF NEEDED.

FOR FDA USE ONLY

Concurrence of Center for Devices and Radiological Health (CDRH) *(Signature)*

Elizabeth A. Stafford -S